



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/584,280

06/26/2006

Kazuyuki Ohmoto

Q95661

4079

65565 7590 06/22/2009
SUGHRUE-265550
2100 PENNSYLVANIA AVE. NW
WASHINGTON, DC 20037-3213

EXAMINER

RODRIGUEZ-GARCIA, VALERIE

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

06/22/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/584,280	Applicant(s) OHMOTO ET AL.	
	Examiner VALERIE RODRIGUEZ-GARCIA	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3 and 5-15 is/are pending in the application.
- 4a) Of the above claim(s) 6 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3,5 and 7-15 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/06/2007, 06/26/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Amendments to the claims have been received on May 15, 2009. Claims 1-2 and 4 were canceled. Therefore, claims 3 and 5-16 are currently pending in this application.

Priority

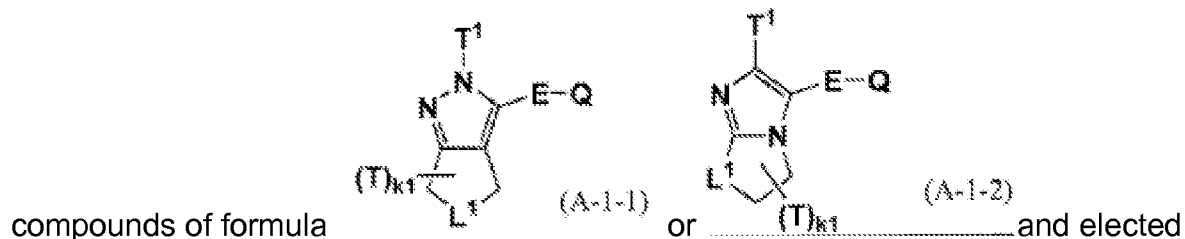
This application is a 371 of PCT/JP2004/019753, filed on December 24, 2004, which claims priority benefit of foreign application JP 2003-433417, filed on December 26, 2003. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

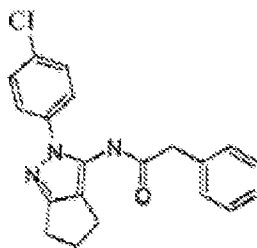
Information Disclosure Statement

The information disclosure statement, filed June 6, 2006, fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because the foreign references are not provided. It has been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Response to Species Election

Applicant's election **without traverse** of Group I, claims 3 and 5-15, drawn to





species compound of Example 8(13)

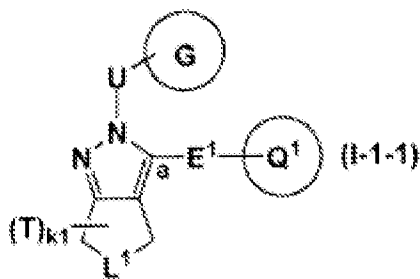
in the reply filed on

05/15/2009 is acknowledged.

Therefore, claim 15 is withdrawn from further consideration pursuant to 37 CFR 1.142 (b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and element and would require separate search considerations.

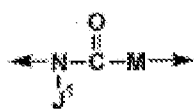
Elected Group I is being examined according to M.P.E.P. § 803.02. The claims within elected Group I have been examined to the extent that they are readable on the elected species of Compound Example 8(13) above. Since no prior art was found on the elected species, the examination was expanded within elected Group I until art was found, in which case, the examination stopped and art has been applied against the claims. Note, M.P.E.P. § 803.02. The subject matter of the expanded search (inclusive of the elected species of Compound Example 8(13)) is as follows:

The scope of the elected invention for search and examination:



Compounds of Formula (I-1-1), , depicted in claim

5, wherein: **L¹ is C1-4 alkylene; G is optionally substituted phenyl; E¹ is**



; Q¹ is optionally substituted phenyl; and U and M are as defined. As

a result of the election and the corresponding scope of the invention identified supra, claim 6 and the remaining subject matter of claims 3, 5 and 7-15 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups such as morpholine, triazole, pyrimidin, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classifications of these functional groups in the U.S. classification system, i.e. class 544 subclass 106(+) (morpholine), class 540 subclass 215(+) (triazoles), 544 subclass 224(+) pyrimidines, etc. Therefore, the subject matter which are withdrawn from consideration as being non-elected subject differ materially in structure and composition and have been restricted properly. A reference which anticipates the elected subject matter would not render obvious the withdrawn subject matter. In addition, the fields of search are not co-extensive.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one

or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The claims embraced by the above expanded search are claims 3, 5 and 7-15.

Pursuant to amendment claims 3 and 5-16 are currently pending, claims 6 and 16 are withdrawn and claims 3, 5 and 7-15 are the subject of this office action. This is the First Action on the merits of the claims.

Claim Rejections - 35 USC § 102

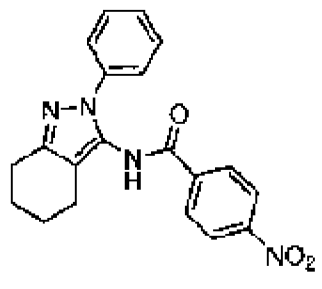
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

1. Claims 3, 5, 7, 8 and 10-15 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by JP 11-171865 A (Yoshitomi Pharmaceutical Industries, June 29, 1999); cited in the International Search Report.

90



JP 11-171865 A describes compound 90
the compounds of Formula (I-1-1) of the scope of the invention above U is a bond, M is

Art Unit: 1626

a bond and L1 is C2 alkylene. Pharmaceutical compositions with carrier or diluent can be found in paragraph [0044], also see claim 7 for an additional (additive) agent.

Instant claims 11-14 recite an intended use of the composition; however, the claims are drawn to the composition. The use of the composition does not bring a limitation into the composition claim.

See MPEP 2112.

**SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE
UPON THE DIS-COVERY OF A NEW PROPERTY**

“[T]he discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art’s functioning, does not render the old composition patentably new to the discoverer.” *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). >In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court held that the claimed promoter sequence obtained by sequencing a prior art plasmid that was not previously sequenced was anticipated by the prior art plasmid which necessarily possessed the same DNA sequence as the claimed oligonucleotides. The court stated that “just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel.”

If the body of a claim fully and intrinsically sets forth all of the limitations of the claimed invention, and the preamble merely states, for example, the purpose or intended use of the invention, rather than any distinct definition of any of the claimed invention’s limitations, then the preamble is not considered a limitation and is of no significance to claim construction. *Pitney Bowes, Inc. v. Hewlett-Packard Co.*, 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999). See also *Rowe v. Dror*, 112 F.3d 473, 478, 42 USPQ2d 1550, 1553 (Fed. Cir. 1997) (“where a patentee defines a structurally complete invention in the claim body and uses the preamble only to state a purpose or intended use for the invention, the preamble is not a claim limitation”); *Kropa v. Robie*, 187 F.2d at 152, 88 USPQ2d at 480-81 (preamble is not a limitation where claim is directed to a product and the preamble merely recites a property inherent in an old product defined by the remainder of the claim); *STX LLC v. Brine*, 211 F.3d 588, 591, 54 USPQ2d 1347, 1350 (Fed. Cir. 2000) (holding that the preamble phrase “which provides improved playing and handling characteristics” in a claim drawn to a head for a lacrosse stick was not a claim limitation). See MPEP 2111.02 (II)

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 11- 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition according to claim 10 with binding affinity to the mitochondrial benzodiazepine receptor, does not reasonably provide enablement for treating or preventing “diseases mediated by the mitochondrial benzodiazepine receptor” and for treating or preventing all the diseases recited in claims 11-14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. There is no reasonable basis for assuming that a pharmaceutical composition comprising the compound of formula (I-1-1) will treat or prevent all the diseases related to the mitochondrial benzodiazepine receptor, neither all claimed diseases caused by stress, which are not even remotely related. Moreover, this is not possible to prove or predict. Note *In re Surrey* 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount

Art Unit: 1626

of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: A pharmaceutical composition comprising a chemical compound of formula (I-1-1), of claim 1 is used for the prevention or treatment of diverse diseases “mediated by the mitochondrial benzodiazepine receptor” such as respiratory system disease, epilepsy, myocardial infarction and many others. In the specification, page 9 and 52-53, other diseases are also included such as cancer and dental disease caused by stress. The clinical use of these compounds and the pharmacokinetic behavior of the claimed substances in the human body are involved.

Breadth of the Claims: The instant invention is complex in that the rejected claims encompass prevention of diseases mediated by mitochondrial benzodiazepine receptor. In other words, a mammal treated according to the recited method can not get any kind of disease or condition mediated by mitochondrial benzodiazepine receptor at any time after administration of the claimed composition or compound. The complex nature of the claims is greatly exacerbated by the disorders to be treated, such as “depression, epilepsy, respiratory disorders, cancer, myocardial infarction” and many unknown, unpredictable and unrelated others disclosed in pages 52-53 that supposedly fall within the “mediated by mitochondrial benzodiazepine receptor”.

Level of unpredictability in the art: The invention is pharmaceutical in nature as it involves a composition for the treatment of many unrelated and diverse disorders (See at least pages 52-53 of the specification). It is well established that “the scope of enablement varies inversely with the degree of unpredictability of the factors involved” and physiological activity is generally considered to be unpredictable. See *In re Fisher* 166 USPQ 18. The lack of significant guidance from the specification or prior art with regards to the actual prevention of diseases such as depression, epilepsy, respiratory disorders, cancer, myocardial infarction, etc., with the claimed compounds makes practicing the claimed invention unpredictable.

Guidance of the Specification: There is no guidance given by the specification as to how one would administer the claimed compounds in order to actually **prevent or** treat the

Art Unit: 1626

claimed diverse and unpredictable diseases in the claims and pages 52-53 supposedly related to mitochondrial benzodiazepine receptor. All of the guidance provided by the specification is directed towards affinity of some compounds to mitochondrial benzodiazepine receptor (p. 76-77), rather than treatment or prevention.

State of the prior art: *Nature Reviews: Drug Discovery* offers a snapshot of the state of the drug development art. Herein, drug development is stated to follow the widely accepted Ehrlich model which includes: 1) development of a broad synthetic organic chemistry program; 2) subsequent testing of compounds in an appropriate laboratory model for the disease to be treated; and 3) screening of compounds with low toxicity in prospective clinical trials (Jordan, V. C. *Nature Reviews: Drug Discovery*, 2, **2003**, p. 205);

The skill of those in the art: The examiner notes that the knowledge of level of skill in this art would not permit one skilled in the medicinal chemistry and pharmacy art to assert an intended use for the pharmaceutical formulation comprising a compound of formula (A-1-1) or (I-1-1), and the skilled artisan would not immediately envisage the invention claimed.

Existence of working examples/specification: There are no working examples in the specification. Experimentation was carried out to see only the receptor binding effect to mitochondrial benzodiazepine receptor in rat brain, not treatment and not prevention. It is impossible to extrapolate the results of the experiment performed (in pages 76-77) to achieve a meaningful conclusion about what diseases could be treated or prevented with the claimed compounds. Applicants have not sufficiently established that the instant invention is effective for treatment or prevention of all the diseases or conditions in claims 11-14 and recited in page 52 of the specification. Currently, a clear evaluation of which diseases or conditions could be treated is needed.

Amount of experimentation necessary: In order to practice the claimed invention one of ordinary skill in the art would have first to investigate a combination of appropriate pharmaceutical carrier, compound dosages, duration of treatment, route of administration, etc. and appropriate animal model system for one of the claimed compounds and test the combination in a model system to determine whether or not the combination is effective for prevention or treatment of the diverse diseases claimed. One of ordinary skill would need to test all the compounds and formulations of claims

Art Unit: 1626

11-14 for their activity, including in vivo, and investigate their bioavailability. One of ordinary skill in the art would have to treat patients that never have had any of the claimed disease or conditions with the claimed compositions and evaluate the patients for the development of ANY disease in order to investigate prevention.

Predicting whether a recited compound is in fact one that produces a desired physiological effect at a therapeutic concentration and with useful kinetics, is filled with experimental uncertainty, and without proper guidance, would involve a substantial amount of experimentation (Jordan, V. C. *Nature Reviews: Drug Discovery*, 2, **2003**, pp. 205-213).

It would require undue experimentation for one of ordinary skill in the art to practice the claimed invention in the full broad scope recited in the claims. Therefore, the claimed invention of a pharmaceutical composition according to claims 11-14 effective for treating or preventing all the different diseases or conditions recited in claims 11-14 is not fully enabled by the instant specification.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make/or use Applicants' invention.

3. Claims 3, 10 and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compounds of formula (A-1-1) and (I-1-1), pharmaceutically acceptable salts and N-oxides thereof, does not reasonably provide enablement for solvates or prodrugs of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557, 1561 (Fed. Cir. 1993). Explaining what is meant by “undue experimentation,” the Federal Circuit has stated:

The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability or unpredictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The nature of the invention is that of a chemical compound, a prodrug of the compound or a pharmaceutical composition comprising that compound, wherein the compound is in a special physical form - solvate. The clinical use of these compounds and the pharmacokinetic behavior of the claimed substances in the human body are involved.

Breadth of the Claims: The “solvates thereof” embodiments of the instant claims read on solvates of the compound according to formula (I) with *any* solvent. The definition of a solvate, taken from the Vippagunta et al. reference, cited in section (3), (4), (5) below, is

Art Unit: 1626

a "crystalline solid adduct[s] containing solvent molecules within the crystal structure, in either stoichiometric or nonstoichiometric proportions, giving rise to unique differences in the physical and pharmaceutical properties of the drug". Solvates are a complex arrangement of a solvent and the compound in claims, and so far the instant claims do not specify the identity of the complexes formed by the claimed compound and the solvent. The instant claims also present an *unknown* list of potential prodrug derivatives.

Guidance of the specification: Aside from a mention that the invention includes solvates and prodrug derivatives in page 34 of the specification, and some basic information about both terms, no guidance relevant to preparation of prodrugs and solvates is provided in the disclosure.

State of the prior art: Solvates, at the time the invention was made, were known to exist, and many had been documented, but the level of skill in the art had not progressed to such an extent that the preparation of those solvates other than hydrates was routine or simple. The following references address the state of the art with respect to crystalline forms of organic compounds, formation of solvates of organic compounds, and the lack of predictability thereof:

Vippagunta et al, "Crystalline Solids", Advanced Drug Delivery Reviews, vol. 48, pages 3-26 (2001).

Gavezzotti, "Are Crystal Structures Predictable?", Accounts of Chemical Research, vol. 27, pages 309-314 (1994).

First, it is evident from both of the references that formation of specific crystalline forms, and more particularly, solvates, is highly unpredictable. See Gavezzotti, page

Art Unit: 1626

309, the first sentence, and page 312, point #8; also see Vippagunta et al, page 11, "Prediction of Polymorphs" and page 18 "Prediction of the formation of hydrates and solvates". Because the formation of solvates is unpredictable, even the high level of skill possessed by a person with a Ph. D. degree and several years of industrial experience is not enough to render preparation of solvates routine. Each solvate of each compound must be experimentally prepared, by a trial and error process (since the conditions necessary for the formation cannot be predicted), and all of the factors relevant to each individual compound's ability to crystallize must be studied. These factors are identified in points #1-7 of the Gavezzotti reference. The preparation of each single claimed solvate represents a significant undertaking in the areas of preparative organic chemistry, physical chemistry, and crystallographic measurements.

With respect to prodrugs, Wolff (Medicinal Chemistry) summarizes the state of the prodrug art (Wolff, Manfred E. "Burger's Medicinal Chemistry, 5ed, Part I", John Wiley & Sons, 1995, pages 975-977). The table on the left side on page 976 outlines the research program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker et al. in the first sentence of third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug (Banker et al, "Modern Pharmaceutics, 3ed.", Marcel Dekker, New York, 1996, pages 451 and 596).

Art Unit: 1626

Existence of working examples/specification: There are no working examples of a prodrug or solvate of a compound represented by the formula (A-1-1) neither (I-1-1).

The skill of those in the art: Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would need to have a Ph. D. degree and several years of industrial experience. However, a person of ordinary skill in the art has bachelor's degree in chemistry with some years of industrial experience. A person of ordinary skill in the art knows how to follow and apply standard and known operating procedures.

The predictability or unpredictability of the art: It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Amount of experimentation necessary: The compound of formula (A-1-1) and (I-1-1) as a solvate with every solvent within the scope of the term "solvate" generally, of which there are also many thousands, would require the efforts of many researchers over a period of years. Those efforts would be potentially inconclusive. For one of skill in the art to conduct the type of research outlined in Gavezzotti and in Vippagunta et al for preparation of every one of the claimed solvates would be undue. Applicants' right to exclude others from making all solvates of compounds according to formulae (A-1-1) and (I-1-1) is unwarranted in light of the lack of any direction as to how one of ordinary skill would do so.

Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed compound, for example, is in fact a prodrug, that produces the active compound metabolically in man at a therapeutic concentration and at a useful rate is

Art Unit: 1626

filled with experimental uncertainty. Although attempts have been made to predict drug metabolism *de novo*, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be clinically effective. Determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

It is concluded that the amount of experimentation necessary for one of ordinary skill to practice the full scope of what is claimed is undue, especially since not one example of a specific solvate or specific prodrug of the compound of the invention has been described, much less actually made. The full scope of the solvates and prodrug embodiments, together, is enormous and would be practically impossible to achieve.

4. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

In the instant case, the term “anxiety drugs, antidepressant drugs, antiparkinson drugs, etc.”, in claim 15 has not been properly disclosed in the application. The disclosure and claim 15 describe the “anxiety drugs, antidepressant drugs, antiparkinson drugs, etc.” by their biological property or function rather than by their structure. Applicants have not specified the “drugs” in claims 15 for which patent protection is being sought. As such, the skilled artisan would not recognize, know how

to make and use the invention. Moreover, the Specification provides only for the use of some drugs in pages 57-58. The Specification does not describe any other compounds so as to convey possession of the entire genus encompassed by the general terms “anxiety drugs, antidepressant drugs, antiparkinson drugs, etc.” in claims 15. As such, instant claim 15 lacks support in the specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 3, 5 and 7-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants recite “binding bond”. The claims are indefinite because it is not clear what is meant by a “binding bond”. A chemical bond is a force connecting or linking atoms. Applicants are suggested to delete “binding”.

In claim 14, the recitation “wherein a central nervous system caused by stress” is unclear. What is a central nervous system caused by stress? Appropriate correction is required.

In claim 15 applicants recite “a pharmaceutical composition combining of the compound...”. What is combining of the compound? In addition, claim 15 recites “and one kind or more kind selected from”. One kind or more kind of what? It is unclear what a kind selected from means. Appropriate correction is required. For a proper Markush

language format the claim should recite “and a compound selected from the group consisting of”.

Claim Objections

6. Claims 3, 5 and 7-15 are objected to as containing non-elected subject matter. Claims 3, 5 and 7-15 presented drawn solely to the elected invention identified supra as **the elected invention for search and examination** would overcome this objection.

Specification Objection - Title

Applicant is reminded of the proper content of the title of the invention.

The title of the invention should be brief, but technically accurate and descriptive, preferably from two to seven words. See 37 CFR 1.72(a) and MPEP § 606.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. In the revised title, the examiner suggests including the name of the main core of the chemical structure and the alleged utility possessed by the compounds applicants regard as their invention.

Specification - Abstract

Applicant is reminded of the proper content of an abstract of the disclosure.

With regard particularly to chemical patents, for compounds or compositions, the general nature of the compound or composition should be given as well as the use thereof, e.g., *The compounds are of the class of alkyl benzene sulfonyl ureas, useful as oral anti-diabetics*. Exemplification of a species could be illustrative of members of the class. For processes, the reaction type, reagents and process conditions should be stated, generally illustrated by a single example, unless variations are necessary. See

Art Unit: 1626

MPEP § 608.01(b), Section B.

The abstract of the disclosure is objected to because: a) it neither provides for the general nature of the compounds nor exemplifies any members or formulae illustrative of its class; and b) should be amended to reflect the scope of the *elected invention for search and examination* above. Correction is required. See MPEP § 608.01(b).

Examiner's Note

The disclosure was not carefully examined for errors. However, several errors were quickly found. See for example: p. 1-2,

Steroid synthesized in the brain is called as neurosteroid. and

progesterone control adversely. Thus, it has been thought that as a result of balance between an excitatory signaling system and an inhibitory signaling system was collapsed by neurosteroid content in the brain varying under stress condition, the

Applicant's assistance is requested in this matter.

Telephone Inquiry

Claims 3, 5 and 7-15 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VALERIE RODRIGUEZ-GARCIA whose telephone number is (571)270-5865. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1626

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kamal A Saeed/
Primary Examiner, Art Unit 1626

/VALERIE RODRIGUEZ-GARCIA/
Art Unit 1626